A COMPARATIVE STUDY OF FINE NEEDLE ASPIRATION CYTOLOGY VERSUS NON-ASPIRATION TECHNIQUE IN THYROID SWELLINGS

Dissertation submitted for the degree of

M.S. (Branch 1) General Surgery

MARCH-2007

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI,
TAMILNADU

CERTIFICATE

This is to certify that the dissertation entitled

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Dissertation titled "A **COMPARATIVE STUDY OF FINE**

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ASPIRATION TECHNIQUE IN THYROID SWELLINGS ",

has been prepared by me in the Department of General Surgery,

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This is submitted to The Tamil Nadu Dr.M.G.R.Medical

University, Chennai, in partial fulfillment of the requirements

for the award of M.S. Degree Examination (Branch 1)

General Surgery to be held in MARCH - 2007.

Place: Madurai.

Date: 20 / 10 / 2006 DR. P. RAJENDRAN

ACKNOWLEDGEMENT

I express my sincere gratitude to the Dean-in-charge, Dr.S.M.Sivakumar M.S, for allowing me to utilize the clinical materials for this study.

Foremost, I wish to express my gratitude to Prof.M.Kalyanasundaram M.S, FICS, Professor & Head of the Department of General Surgery for his valuable support and continued guidance.

My sincere thanks to Prof.M.Gobinath M.S, unit chief for his valuable guidance, encouragement and support in completing this study.

I express my sincere thanks to Prof. Gomathi Nayagam M.D, Professor and Head of the Department of Pathology, for his support and guidance.

I sincerely thank all the unit chiefs and Assistant Professors of the Department of General Surgery, for their co-operation and guidance.

I owe my sincere thanks to all the patients for their kind co-operation in the study.

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TABLE OF CONTENTS

INTRODUCTION

Fine Needle Biopsy (FNB) is defined as using a fine needle to remove a sample of cells from a suspicious mass for diagnostic purposes.

Fine needle cytology has proven to be an effective first line diagnostic tool in evaluating palpable thyroid lesions. It allows better selection of the patients who need to undergo a surgical procedure, and also helps in deciding what surgery to be performed. It can be performed quickly and painlessly in the outpatient department without the need for local anesthetic. One can sample nodules as small as 1 cm and even smaller if the nodule is easily accessible. Skill in the interpretation of FNB specimens is readily acquired by qualified cytopathologists after study of reference material and the acquisition of reasonable experience.

The advantages of FNB are summed up in the acronym **SAFE**: it is **S**imple, **A**ccurate, **F**ast, **E**conomic, and, indeed, safe.

FNB is not, however, a substitute for conventional surgical Histopathology. Instead, it should be regarded as a component of the pretreatment study of pathological processes in combination with clinical, radiological, and other laboratory data.

The fears that led to hesitation about thyroid FNB have not been borne out. They included doubt that the number of thyroid operations would be reduced, concern that there would be a significant number of thyroid cancers missed because of false-negative FNB results, and worry that tumor could be seeded along a needle track. Seeding has been described only in two reports involving large-needle biopsies and one FNB.

However, in aspiration of thyroid lesions, an unsatisfactory specimen, especially mixed with blood, poses an obstacle in proper cytological interpretation.

In an attempt to overcome the problem of vascularity of the thyroid gland, an alternative fine needle sampling method was developed in France. It avoids aspiration, utilizes only the needle and relies on capillary pressure to suck the cells inside the needle bore. This technique of Fine Needle Capillary Sampling (FNC) was termed as Cytopuncture by Brifford [14] in 1982.

ANATOMY OF THYROID

Leonardo da vinci originally depicted the thyroid in his drawings as two separate glands on either side of the larynx. The term thyroid (Greek thyreoeides, shield shaped) was given by Thomas Wharton in his Adenographia (1656).

The Thyroid Gland (Glandula Thyreiodea; Thyroid Body) is a highly vascular organ, situated at the front and sides of the neck; it consists of right and left lobes connected across the middle line by a narrow portion, the isthmus. It weighs usually about 30 grams.

The lobes (lobuli gl. thyreoideæ) are conical in shape, the apex of each being directed upward and lateralward as far as the junction of the middle with the lower third of the thyroid cartilage; the base looks downward, and is on a level with the fifth or sixth tracheal ring. Each lobe is about 5 cm. long; its greatest width is about 3 cm., and its thickness about 2 cm. The lateral or superficial surface is convex, and covered by the skin, the superficial and deep fasciæ, the Sternocleidomastoideus, the superior belly of the Omohyoideus, the Sternohyoideus and Sternothyreoideus, and beneath the last muscle by

the pretracheal layer of the deep fascia, which forms a capsule for the gland. The deep or medial surface is moulded over the underlying structures, viz., the thyroid and cricoid cartilages, the trachea, the Constrictor pharyngis inferior and posterior part of the Cricothyreoideus, the esophagus (particularly on the left side of the neck), the superior and inferior thyroid arteries, and the recurrent nerves. The anterior border is thin, and inclines obliquely from above downward toward the middle line of the neck, while the posterior border is thick and overlaps the common carotid artery, and, as a rule, the Parathyroids.

The isthmus (isthmus gl. thyreoidea) connects together the lower thirds of the lobes; it measures about 1.25 cm. in breadth, and the same in depth, and usually covers the second and third rings of the trachea. In the middle line of the neck it is covered by the skin and fascia, and close to the middle line, on either side, by the Sternothyreoideus. Across its upper border runs an anastomotic branch uniting the two superior thyroid arteries; at its lower border are the inferior thyroid veins.

A third lobe, of conical shape, called the pyramidal lobe, frequently arises from the upper part of the isthmus, or from the adjacent portion of either lobe, but most commonly the left, and ascends as far as the

hyoid bone.

A fibrous or muscular band is sometimes found attached, above, to the body of the hyoid bone, and below to the isthmus of the gland, or pyramidal lobe. When muscular, it is termed the Levator glandulæ thyreoideæ.

HISTOLOGY OF THYROID

Microscopically, the thyroid gland is made up of round or oval follicles, with an average diameter of 200 μm. They are lined by a single layer of follicular cells whose shape ranges from flattened to low columnar depending on their degree of activity. The cytoplasm has a pale acidophilic or amphophilic staining quality; the greater the activity of the cell, the greater its amount. Follicular cells with abundant granular acidophilic cytoplasm are referred to as Hürthle cells (a misnomer), Askanazy's cells, oxyphilic cells, or oncocytes.

Ultrastructurally, this granularity is due to the accumulation of mitochondria. They can be detected immunohistochemically with antibodies directed against mitochondrial enzymes.

The main ultrastructural features of follicular cells are abundant granular endoplasmic reticulum, a well-developed Golgi apparatus, lysosomes

(particularly numerous in actively secreting cells, and mainly located toward the apical side), and numerous microvilli in the luminal border. The intra-luminal colloid is pale staining and with scalloped borders in follicles with active secretory function and densely eosinophilic in inactive ones. It is

variably PAS positive and alcianophilic, depending on the types and relative amounts of carbohydrate components present. Birefringent calcium oxalate crystals may be found, their number increasing with age. Collections of small follicles protruding into the lumen of larger follicles are commonly seen in actively secreting glands; they are sometimes referred to as Sanderson's polsters.

Immunohistochemically, reactivity for thyroglobulin, triiodothyronine (T3), and thyroxine (T4) is found both in the colloid and in the cytoplasm of the follicular cells. Thyroglobulin is the most useful of these markers.

Neuroendocrine cells of presumed neural crest derivation known as C cells or Parafollicular cells represent the other major epithelial component of the thyroid gland. The latter term is a misnomer, because immunohistochemical and ultrastructural studies have shown that they occupy an exclusively intrafollicular position. C cells are restricted to the middle and upper thirds of the lateral lobes along their central axes. The number of C cells varies

according to age; they are more numerous in infancy and old age than in adults.

Ultrastructurally, C cells contain numerous dense-core granules of neurosecretory type. They are argyrophilic with the Grimelius reaction; metachromatic with toluidine blue; and positive for lead hematoxylin.

EVOLUTION OF THYROID CYTOLOGY

For over 100 years the discipline of Pathology was essentially diagnostic Histopathology and this in turn on surgical biopsy. For the last 60 years, exfoliated and abraded sample of cells have also been collected from accessible anatomical surfaces, especially from the uterine cervix and the bronchus. Thus a diagnostic discipline has arisen in parallel with Histopathology which subserves both a screening and predictive function.

In 1883 Leyden et al [10] and 3 years later Menetrier [11] employed needles to obtain cells and tissue fragments, the former to isolate pneumonic microorganisms and the latter to diagnose pulmonary carcinoma.

In 1919 Hirshfeldt H et al [12] study revealed the wide acceptance of needling the bone marrow an integral part of the investigation of hematological problems which continued to serve as a remainder that almost every tissue could be sampled by an easily acquired technique requiring neither

anesthesia nor the surgical intervention.

Almost 70 years ago, Fred Stewart, a surgical pathologist at the Memorial Hospital Laboratory in New York, published the results of 2,500 tumors biopsied by an aspiration method using an 18-gauge needle. Stewart's report marked the onset of needle aspiration in the U.S. as a form of biopsy.

The concept of FNAC for thyroid swellings was first introduced by Martin & Ellis (1930) at the Memorial Sloan – Kettering Hospital, who used an 18-gauge needle aspiration technique. Subsequently, cutting needle biopsy using Silverman or Tru-Cut needles was used for tissue examination. None of these techniques gained wide acceptance because of fear of malignant implants in the needle track, false-negative results, and serious complications.

True fine needles for aspiration (22- to 27-gauge vs. 18-gauge) were first introduced by Lopez-Cardozo in The Netherlands and Soderström in Sweden in the 1950s. At that time, the European clinicians developed the use of Romanowsky and May-Grünwald Giemsa stains (similar to Diff-Quick or Wright's stain for blood smears) for use on air-dried smears to allow for rapid interpretation. Despite their success, it was not until the 1980s that fine-needle aspiration (FNA) biopsy became popular in the U.S.

In 1981 Ashcraft and van Herle exhaustively reviewed preoperative

diagnostic techniques for thyroid nodules and concluded that needle biopsy was the best of those available, but skepticism was expressed as late as 1984.Since then, FNB has gained progressively wider acceptance, including endorsement by the American Thyroid Association and the American Association of Clinical Endocrinologists, and is now in general use because its advantages have been confirmed. Currently, this technique is practiced worldwide.

In India, the technique was first introduced at Chandigarh in the early seventies followed by AIIMS, New Delhi, in the mid seventies. The first major study by an Indian was the one done by Rao S K et al [13], in which about 341 cases of solitary thyroid nodules were evaluated over a period of 10 years.

The technique of Non Aspiration Cytology for thyroid lesions was first evaluated and compared with the conventional FNAC by Santos and Leiman (1988) in 50 nodular lesions.

Since then numerous studies have been conducted and many are still being under evaluation to assess the advantages if any of this technique over the conventional aspiration technique.

CYTOPATHOLOGY

BENIGN NON-NEOPLASTIC LESIONS:

Chronic Lymphocytic Thyroiditis:

Fine needle aspirates from autoimmune (Hashimoto's) thyroiditis are generally moderately cellular, characterized by a mixed population of mature and transformed lymphocytes, plasma cells, histiocytes, and occasional tingible-body macrophages. This inflammatory component is accompanied by aggregates of follicular cells, Hürthle cells, and scant colloid. Difficulties can be encountered in distinguishing between lymphocytic thyroiditis and Hürthle cell neoplasm. Lymphomas arising in the setting of Hashimoto's thyroiditis are most often large cell type and may be recognized in aspirate material by a monotonous population of large

atypical lymphoid cells. The FNA finding of a predominant and/or atypical lymphoid population in the setting of Hashimoto's thyroiditis should prompt immunophenotyping evaluation either by immunocytochemistry or flow cytometry.

Nodular Goiter:

Fine needle aspirations from nodular goiter yield abundant colloid, scant to moderate amounts of follicular epithelium, appearing predominantly as flat sheets, occasionally accompanied by Hürthle cell change, and a variable reactive component consisting of macrophages, fibroconnective tissue and inflammatory cells. Aspirates of hyperplastic nodules exhibit a more abundant epithelial component that retains bland, uniform morphology and a background of abundant colloid. The reactive component predominates in aspirates of hemorrhagic cysts, yielding numerous hemosiderin-laden macrophages along with abundant colloid. However, it should be noted that up to 15% of cystic lesions might represent cystic degeneration of a neoplasm, most commonly papillary carcinoma. This highlights the importance of repeat sampling of any solid areas remaining after cyst

drainage, and provides a rationale for surgical removal of large, persistent cysts.

NEOPLASTIC LESIONS :

Follicular Neoplasm:

Fine needle aspiration specimens from follicular neoplasm's are cellular with scant to absent colloid. The follicular epithelium appears in syncytial fragments with microfollicular or trabecular patterns. Both morphologic and morphometric studies have emphasized the features of increased nuclear size, nuclear pleomorphism, and crowding as helpful in the specific cytological diagnosis of follicular carcinoma. However, in routine practice, most follicular carcinomas and follicular adenomas have a similar cytological pattern. This pattern may be indistinguishable, in 15% to 25% of cases, from hyperplastic nodule in goiter. Similarly, overlapping cytological criteria occur between follicular neoplasm and follicular variant of papillary carcinoma, particularly when the characteristic nuclear changes are focal and not adequately sampled, or are poorly visualized in the aspirated material.

Generous sampling and optimal specimen preparation minimize these limitations of FNA in distinguishing among follicular lesions. Overall, the incidence of malignancy in nodules with a cytological diagnosis of follicular neoplasm ranges from 15% to 22%.

Hürthle Cell Neoplasm:

Hürthle cell neoplasm aspirates are cellular, with scant colloid, and contain cells with abundant, granular cytoplasm and central round nuclei that often have prominent nucleoli. The cells are loosely cohesive, appearing in aggregates, singly, in monolayers, or follicular patterns. Marked nuclear atypia, binucleation, and eccentric nuclei may be common in both adenomas and carcinomas and cannot be used as indicators of malignancy. Ordinary follicular cells are scarce (<10%) and a lymphocytic infiltrate is absent. The differential diagnosis includes chronic lymphocytic thyroiditis, medullary carcinoma, and, rarely, papillary carcinoma (particularly tall cell, Hürthle cell, or Warthin tumor-like variants).

Papillary Carcinoma:

Fine needle aspirate specimens from papillary carcinomas show a wide range of cytological patterns. High cellularity is a common feature, and colloid is usually scant. The epithelium may appear as true papillary fragments, but more commonly is arranged in multilayered syncytial fragments or branched sheets. A predominant follicular pattern can be seen,

particularly in the follicular variant of papillary carcinoma. Nuclear enlargement and pleomorphism are present, along with nuclear crowding, finely powdery chromatin, nuclear grooves, and sharply defined intranuclear cytoplasmic inclusions that gives the appearance of Orphan Annie eyed nuclei. The cytoplasm is usually dense and cyanophilic. Strict attention must be paid to finding a set of diagnostic criteria, rather than single isolated features, to arrive at the proper diagnosis. The features of multinucleated giant cells, seen in 55% to 100% of cases, and psamomma bodies, while not specific for papillary carcinoma, are helpful associated findings. There is little evidence that the various subtypes of papillary carcinoma can be reliably distinguished in cytological specimens.

Medullary Carcinoma:

Fine needle aspirates from medullary carcinoma are generally highly cellular, composed of loosely cohesive sheets and nests of cells. Occasionally, paucicellular specimens obscured by blood are encountered. The tumor cells have abundant, granular cytoplasm that appears ill-defined and contains small eosinophilic granules on Romanowsky-stained preparations in 5% to 20% of cells. Eccentrically placed, round nuclei impart

a plasmacytoid look to the cells in some medullary tumors, while in others a more spindled or pleomorphic morphology predominates. The nuclear chromatin is coarsely or finely stippled and intranuclear cytoplasmic inclusions may be seen. In the minority of aspirates, the epithelial component is accompanied by amyloid appearing as amorphous globules or irregularly shaped fragments, resembling colloid. Positive immunohistochemical staining for calcitonin is highly specific for medullary carcinoma; however, sensitivity may be as low as 55% to 60% in cytological material.

Anaplastic Carcinoma:

The cytological pattern of these tumors is highly varied similar to it’s histological picture, but marked cellular pleomorphism and anaplasia, accompanied by a necrotic, inflammatory background, are the hallmarks.

Other Malignancies:

The thyroid gland may be a primary site of lymphoma, or secondarily involved by systemic disease.

Most thyroid gland lymphomas are of the large cell type, and appear cytologically as a monotonous population of round cells with scant cytoplasm, finely granular chromatin, and prominent nucleoli. Background features of cytoplasmic fragmentation (lymphoglandular bodies) and karyorrhexis suggest that the abnormal cells are of lymphoid origin, but special immunophenotyping studies are used to confirm monoclonality.

Metastatic tumors to the thyroid gland make up a small proportion of thyroid malignancies. Over a 25-year period at the Mayo Clinic 2.6% of thyroid malignancies were metastatic tumors from other sites. Lung, kidney, breast, and malignant melanoma are reported to be the most common primary sites to metastasize to thyroid, followed by isolated cases from a

wide variety of sites. Yet the majority of thyroid nodules (71%) that develop in patients with known prior malignancy are benign; thus, FNA can play a particularly important role in these patients.

FINE NEEDLE BIOPSY

SELECTION OF NEEDLE:

Twenty-five–gauge, 1½-inch needles produce excellent specimens and are less likely to cause bleeding that dilutes specimens and thereby greatly reduces their usefulness. The ease with which bleeding is induced depends not only on needle size but also on the structure of the nodule. Occasionally, 22- or 23-gauge needles may be best for particularly hard papillary carcinomas and other fibrotic nodules. Larger needles (23-gauge) may be used to drain cysts, followed by reaspiration of any remaining solid areas with a 25-gauge needle.

POSITIONING THE PATIENT:

The patient lies supine, with a pillow under the shoulders to facilitate neck extension and is asked not to talk or swallow while the needle is in the neck. The skin is cleaned with alcohol.

APPROACH:

The operator stands on the side of the patient opposite to that of the thyroid nodule. Current regulations require the use of gloves because of concern about blood-borne diseases. The fingers of one hand fix the nodule, and the needle in the other hand is inserted perpendicular to the anterior surface of the neck. The angle of approach is medial to lateral, placing the needle below the strap muscles and in front of the trachea, making short, rapid strokes with only slight changes in direction.

SPECIMEN ADEQUACY:

Several factors influence non-diagnostic rates for FNB results, including the skill of the operator, vascularity of the nodule, criteria used to judge adequacy of the specimen, and the cystic component of the nodule.

Studies have shown average insufficiency rates in the 15% to 20% range. The non-diagnostic thyroid aspirate can pose a dilemma in clinical management, with cancer rates of 4% to 9% among non-diagnostic thyroid FN Biopsies.

On-site microscopic assessment, with reaspiration when necessary, can minimize the number of inadequate specimens. Reaspiration yields satisfactory specimens in at least 50% of cases that are considered non-diagnostic on initial FNB. Although it has been suggested that more aspirations will increase the diagnostic rates, the optimal number of aspirations is a matter of debate. In general, most reports indicate that two to four aspirates per nodule are adequate.

While it is generally agreed that the presence of follicular cells is a minimum requirement for thyroid cytology adequacy, the absolute number of cells is subject to debate.

Some authors propose adequacy criteria of five to six groups of well-preserved follicular cells, with each group containing ten or more cells. Others require eight to ten fragments of well-preserved follicular cells on at least two smears.

To increase chances of adequate cellular material, at least six separate specimens that appear grossly satisfactory are necessary. Preferably, the

aspirates should be obtained from the peripheral areas and different parts of the nodule, in a sequential manner, to ensure representative sampling. For larger nodules, the deep center of the mass should be avoided because it is more likely to contain degeneration and fluid, decreasing the chance of a diagnostic specimen. For cystic lesions, the fluid should be completely aspirated and FNA attempted on residual tissue.

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC):

A 10-mL syringe is used, the plunger is withdrawn about two thirds of the way to produce negative pressure, and one looks for fluid in the needle hub. At the first appearance of fluid, negative pressure is released and the needle withdrawn. No fluid should enter the syringe. If this happens, the specimen will be too dilute and may be lost in the syringe.

Material may appear in the syringe if too large a needle is used, if negative pressure is too vigorous, if the nodule is extensively degenerated or unusually vascular, or if the nodule is cystic. For the first two possibilities, adjustments can be made to improve the chances for success with subsequent punctures. The last two situations are beyond control, although it may help to insert the needle at the nodule periphery, where degeneration is

less likely.

The initial aspiration may produce no specimen if the needle is not in the nodule, if the needle is too fine, if negative pressure is not vigorous enough, or if the nodule is fibrotic. If negative pressure fails to produce fluid, the simplest method to disrupt the tissue is to move the needle in and out within the nodule through a vertical distance of 1 to 2 mm. This maneuver nearly always yields a specimen, but if not, one can combine in-and-out movement with rotation of the needle, to sever small tissue fragments. If the nodule is purely cystic, it will collapse with aspiration. If there is a solid component, FNB samples should be taken from any residual mass. Examining the sediment from cyst fluid rarely yields useful information.

FINE NEEDLE NON ASPIRATION CYTOLOGY (FNNAC):

It relies on the property of capillary tension in narrow channels. This physical principle states that a fluid (or semi fluid substance) will ascend spontaneously into a narrow tube in inverse proportion to the diameter of that tube. The needle is held in a pencil grip, which facilitates precise needle placement for small nodules, and allows the needle to be moved both in and out over a few millimeters and rotated. This combined motion uses the bevel

of the needle for cutting, which frees cells that flow into the needle by capillary action while the needle is held steady for about 10 seconds. Material entering the hub of the needle is readily visible.

SMEAR PREPARATION :

Slides are labeled and placed on the table before aspiration, ready for use. Five milliliters of air is aspirated into the syringe, and the needle placed on the syringe. With needle bevel pointing down, one drop of aspirated material is expelled onto each of several glass slides A grossly satisfactory FNB specimen consists of a small amount of red-orange fluid. Smears are prepared in a manner similar to that for blood smears, in which a second slide is held at a 45- to 60-degree angle to the specimen on an underlying slide. The specimen is allowed to spread out along the edge of the upper slide, which is then advanced along the lower slide, drawing the specimen into a smear. This method may produce thick, uneven smears.

The following alternative maneuver produces flat, uniformly dispersed smears: a top slide is placed flat on the bottom, specimen slide, and, with the index finger, the top slide is pressed down onto the specimen and drawn

over the bottom slide.

Slides are then immediately wet-fixed by placing them in alcohol bottle. Air-dried smears are often prepared with a Romanovsky stain. Some pathologists use air-dried smears stained with a modified Romanovsky stain called May-Giemsa-Grünwald (MGG) stain, which enhances cytoplasmic detail, but most American cytopathologists prefer the crisp nuclear detail obtained with the Papanicolaou stain, which needs immediate fixation, before air drying takes place. In some centers FNB specimens are expelled from the needle directly into a fixative/preservative solution, and slides are later prepared in the laboratory. This permits the use of methods that concentrate the thyroid cells and eliminate red blood cells.

POST PROCEDURE OBSERVATION:

After the biopsy has been completed, firm pressure is applied to biopsy site(s) with gauze pad. Once bleeding has stopped, an adhesive bandage (Band-Aid) is placed on the puncture site(s) and the patient is observed for a few minutes and, if there are no problems, allowed to leave.

OTHER USES OF THYROID FNB:

If the rare entity of acute suppurative thyroiditis is suspected, FNB can provide material for Gram stain and culture.

Special stains have identified Pneumocystis carinii as the cause of both painful and painless thyroid enlargement in patients with the acquired immune deficiency syndrome.

One research study described a mutation in the thyroid-stimulating hormone receptor gene in autonomously functioning thyroid adenomas, using RNA obtained by FNB as a template for complementary DNA synthesis, followed by polymerase chain reaction amplification.

ANCILLARY STUDIES:

Effective criteria for the cytologic diagnosis of thyroid lesions are well established, yet areas of diagnostic uncertainty remain. This has led to a search for useful markers of thyroid malignancy that can be applied to cytologic specimens. Studies of vimentin, lectins, and different molecular weight cytokeratins as indicators of thyroid malignancy have met with only limited success, particularly in cytologic material. More promising results were reported in studies describing the immunodetection of the enzyme thyroperoxidase (TPO) in fine needle aspirates of thyroid

malignancies. CD44, lactoferrin, and HBME-1 are other markers with specificity for thyroid malignancies in preliminary studies.

SEQUELAE OF THYROID FNB:

A range of tissue effects has been described in thyroid resections following FNB. The observed tissue alterations are grouped into acute (within 3 weeks of FNB) and chronic categories.

The acute changes include hemorrhage, granulation tissue, giant cells, hemosiderin-laden macrophages, necrosis, and, rarely, infarction [16]. Among the chronic changes are various types of metaplasia (oncocytic, spindle cell, and squamous), linear fibrosis, infarction, pseudo-invasion of the capsule, random nuclear atypia, and papillary degeneration.

In a comprehensive review of 3,000 thyroidectomies, LiVolsi and Merino[15] observed post–fine needle biopsy changes in 300 cases. Others have reported similar rates of tissue damage. These reports highlight the critical importance of providing information on prior fine needle aspiration procedure and the cytological diagnosis to the pathologist handling subsequent tissue samples of a thyroid nodule.

LIMITATIONS OF THYROID NEEDLE BIOPSY:

The principal limitation is inexperience, both in obtaining adequate specimens and in interpreting the specimens.

FNB is not applicable to all nodules. Some are too small and too inaccessible for accurate needle placement, or too far down in the chest to be aspirated safely. Others are so degenerated that useful material cannot be obtained.

Several authors have discussed the problem of follicular neoplasm. Kini believes that follicular adenomas and follicular carcinomas usually can be differentiated on the basis of nuclear size but Hürthle cell lesions are problematic to diagnose cytologically. Other pathologists maintain that benign and malignant follicular/Hürthle cell tumors cannot be distinguished on the basis of aspirated cells only as it requires the demonstration of vascular or capsular invasion and the lesion must be removed for histopathologic examination.

Recent studies suggest that immunohistochemical and genetic markers may be useful in improving diagnostic accuracy in this group. Two such markers, HBME-1 and galectin-3, have shown most promise.

Hypercellular specimens from follicular or Hürthle cell lesions may have features suggestive of, but not diagnostic for, malignancy. Thus, the cytopathologist labels these "suspicious for malignancy" because cytological

features neither confirm nor rule out malignancy. Histological examination is necessary for definitive diagnosis.

Finally, FNB diagnosis of benign for one nodule says nothing about other nodules, whether palpable or impalpable.

POTENTIAL COMPLICATIONS OF NEEDLE BIOPSY:

Occasionally, there is a local hematoma after FNB. An ice pack is adequate treatment. Rarely, the entire thyroid gland swells acutely; this spontaneously resolves within 24 to 48 hours or less. The use of anticoagulants or salicylates does not preclude FN Biopsy.

Seeding a malignancy in the needle track has been reported very rarely after large needle biopsies but had no unfavorable impact on prognosis.

Although FNB, like an ordinary venipuncture, is a clean rather than strictly sterile procedure, infection has not been reported with thyroid FNB.

If the needle enters the trachea, which occasionally happens when a medially situated nodule is sampled, the specimen consists of mucus and air, and the patient may cough, but no harm is done.

If a serum thyroglobulin measurement is desired, it should be done on blood

drawn either before or at least 10 to 14 days after thyroid FNB because the serum thyroglobulin concentration can increase substantially after FNB.

The social and legal consequences of false-positive or false-negative diagnoses are of concern.

AIM OF THE STUDY

- To assess the efficacy and accuracy of fine needle aspiration cytology and non aspiration cytology in evaluation of thyroid malignancies in correlation with histological diagnosis.

- To compare the two techniques with regard to diagnostic yield and quality of smear obtained ,especially with regard to malignant smears.

MATERIALS AND METHODS

The study was undertaken in the Department of General Surgery and the Department of Pathology, Madurai Medical College, Madurai, Tamil Nadu, India for a period of 25 months, from June 2004 to June 2006.

The design of the study was cross sectional diagnostic test evaluation.

All patients with thyroid swellings treated by the surgical units of Government Rajaji Hospital either as outpatients or inpatients during the above study period were randomly divided into two groups.

For one group, cytology smear was obtained by aspiration technique, and for the other group the smears were obtained by non-aspiration technique. The relevant clinical details of these patients were also obtained for the purpose of the study.

25 gauge, 1-½ inch needles were used for obtaining smears by both

Aspiration and Non aspiration techniques (10 ml syringes were used for aspiration technique). Smears were fixed in 95% alcohol for Papanicolaou and Haematoxylin & Eosin staining.

All the smears were obtained by a single observer. The smears were reported by cytopathologist, blinded to the technique employed.

All the smears in both the category, which had the corresponding postoperative Histopathological diagnosis, were included for the study purpose. This amounted to 141 smears in the Aspiration group and 148 smears in the Non aspiration group.

For histological examination, specimens were fixed in formalin. After paraffin embedding, 5-micron thick sections were made and attained with H & E and PAP stains. Special stains were used as and when required (Congo red for demonstration of amyloid in cases of medullary carcinoma).

The cytology smears were classified into one of the five categories for diagnostic purpose by the cytopathologist. In addition the smears were classified into one of the three categories described below with regards to the quality of smear by the cytopathologist.

The cytology diagnosis were tabulated with respect to the corresponding

postoperative Histopathological diagnosis in both categories and the efficacy of cytology smear interpretation in relevance to diagnosis of thyroid swellings in particular the malignancies were evaluated by specific parameters namely sensitivity, specificity, accuracy, percentage of false negatives & false positives.

SMEAR CLASSIFICATION

PATHOLOGICAL CLASSIFICATION:

THY I : Inadequate / unsatisfactory / non diagnostic

THY II : Non neoplastic and benign thyroid lesions

THY III : Follicular neoplasms

THY IV : Suspicious of malignancy

THY V : Diagnostic of malignancy

QUALITATIVE CLASSIFICATION:

Unsuitable specimens(UNS): consisted mainly of red blood cells or absent cellularity making them inadequate for cytodiagnosis.

Diagnostically adequate(DA): possible to render an opinion on the nature

of the lesion sampled, but the cellular material present was sub-optimal due to poor cellularity, sample dilution, degenerative changes or specimen entrapment in blood clots.

Diagnostically superior(DS): Cell aggregates were prominent, well-preserved, unobscured by blood and cell morphology was well displayed.

EVALUATION OF CYTOLOGY

The efficacy of cytology study as a diagnostic / screening tool for thyroid malignancy is evaluated by calculation of the following parameters:

CYTOLOGY REPORT	HPE REPORT		
	MALIGNANT	NON MALIGNANT	
POSITIVE	a(true positive)	b(false positive)	a + b
NEGATIVE	c(false negative)	d(true negative)	c + d
	a + c	b + d	a+b+c+d

Sensitivity = a / (a+c) x 100

Specificity = d / (b+d) x 100

Accuracy = a + d / (a+b+c+d) x 100

Percentage of false negatives = c / (a+c) x 100

Percentage of false positives = b / (b+d) x 100

OBSERVATION

- Total number of cases studied = 289

AGE INCIDENCE:

AGE	BENIGN	MALIGNANT	TOTAL CASES
< / = 20 YRS	24	-	24 (8.3 %)
21 – 30 YRS	86	14	100 (34.6 %)
31 – 40 YRS	40	45	85 (29.4 %)
41 – 50 YRS	12	34	46 (15.9 %)
51 – 60 YRS	7	18	25 (8.7 %)
> 60 YRS	1	8	9 (3.1 %)
TOTAL	170	119	289

SEX INCIDENCE:

	BENIGN	MALIGNANT	TOTAL
MALES	11	23	34 (12 %)
FEMALES	159	96	255 (88 %)
TOTAL	170	119	289

HISTOLOGICAL DIAGNOSIS:

HPE DIAGNOSIS	NO. OF CASES	TOTAL
FOLLICULAR ADENOMA	123 (42.6 %)	BENIGN 170(58.8 %)
MULTINODULAR GOITRE	31(10.7 %)	
HASHIMATO'S THYROIDITIS	16(5.5 %)	
PAPILLARY CARCINOMA	83(28.8 %)	MALIGNANT
FOLLICULAR CARCINOMA	24(8.4 %)	
MEDULLARY CARCINOMA	5(1.7 %)	
ANAPLASTIC CARCINOMA	3(1 %)	

POORLY DIFFERENTIATED CARCINOMA	3(1 %)	119(41. 2 %)
SPINDLE CELL SARCOMA	1(0.3 %)	

SMEAR & HPE REPORT ANALYSIS

ASPIRATION CYTOLOGY (n =141) :

CYTOLOGY DIAGNOSIS:

THY I	20	14.18%
THY II	16	11.37%
THY III	51	36.17%
THY IV	14	9.92%
THY V	40	28.36%

SMEAR QUALIFICATION:

UNS	20	14.18%
DA	98	69.56%
DS	23	16.26%

HISTOLOGY DIAGNOSIS:

Follicular adenoma --- 6 4 (45.39%)

Non-neoplastic	--- 21 (14.89%)
MNG	-- 12
Hashimato's thyroiditis	-- 9
Papillary carcinoma	--- 40 (45.39%)
Follicular arcinoma	--- 11 (7.8%)
Medullary carcinoma	--- 2 (1.42%)
Anaplastic carcinoma	--- 1 (0.71%)
Poorly differentiated carcinoma	--- 1 (0.71%)
Spindle cell sarcoma	--- 1 (0.71%)

SMEAR & HPE REPORT ANALYSIS

NON ASPIRATION CYTOLOGY (n =148) :

CYTOLOGY DIAGNOSIS:

THY I	3	2.02%
THY II	23	15.54%
THY III	61	41.22%
THY IV	15	10.14%
THY V	46	31.08%

SMEAR QUALIFICATION:

UNS	3	2.02%
DA	79	53.37%
DS	66	44.59%

HISTOLOGY DIAGNOSIS:

Follicular adenoma	--- 59 (39.86%)
Non-neoplastic	--- 26 (17.57%)
MNG	-- 19
Hashimato's thyroiditis	-- 7
Papillary carcinoma	--- 43 (29.05%)
Follicular carcinoma	--- 13 (8.78%)
Medullary carcinoma	--- 3 (2.02%)
Anaplastic carcinoma	--- 2 (1.35%)
Poorly differentiated carcinoma	--- 2 (1.35%)

SMEAR QUALITATIVE ANALYSIS

ASPIRATION CYTOLOGY:

SMEAR QUALITY	CYTOLOGY REPORT		TOTAL
	MALIGNANT (n=40)	NON MALIGNANT (n=81)	
DIAGNOSTICALLY ADEQUATE	33 (82.5%)	65 (80.25%)	98
DIAGNOSTICALLY SUPERIOR	7 (17.5%)	16 (19.75%)	23

TOTAL	40	81	121

SMEAR QUALITATIVE ANALYSIS

NON ASPIRATION CYTOLOGY:

SMEAR QUALITY	CYTOLOGY REPORT		TOTAL
	MALIGNANT (n=46)	NON MALIGNANT (n=99)	
DIAGNOSTICALLY ADEQUATE	27 (58.7%)	52 (52.53%)	79
DIAGNOSTICALLY SUPERIOR	19 (41.3%)	47 (47.47%)	66

TOTAL	46	99	145

CYTOLOGY & HPE CORRELATION

ASPIRATION CYTOLOGY:(n =141)

SMEAR CATEGORY	NO. OF SMEARS	HPE DIAGNOSIS								
		HASHI	MNG	FOLL. ADENO	PAP. CA	FOLL. CA	MED. CA	ANA. CA	POOLY DIFF. CA	SPINDLE CELL SAR.
THY I	20	-	-	18	1	-	-	-	-	1
THY II	16	5	8	2	1	-	-	-	-	-
THY III	51	1	1	44	-	5	-	-	-	-
THY IV	14	2	3	-	-	6	2	-	1	-
THY V	40	1	-	-	38	-	-	1	-	-
TOTAL	141	9	12	64	40	11	2	1	1	1

CYTOLOGY & HPE CORRELATION

NON ASPIRATION CYTOLOGY:(n =148)

SMEAR CATEGORY	NO. OF SMEARS	HPE DIAGNOSIS							
		HASHI	MNG	FOLL. ADENO	PAP. CA	FOLL. CA	MED. CA	ANA. CA	POOLY DIFF. CA
THY I	3	-	1	1	1	-	-	-	-
THY II	23	5	14	3	1	-	-	-	-
THY III	61	-	-	55	-	6	-	-	-
THY IV	15	1	3	-	1	7	2	-	1
THY V	46	1	1	-	40	-	1	2	1
TOTAL	148	7	19	59	43	13	3	2	2

EFFICACY OF CYTOLOGY IN DIAGNOSIS OF MALIGNANCY

ASPIRATION CYTOLOGY :

CYTOLOGY REPORT	HPE REPORT		TOTAL
	MALIGNANT	NON MALIGNANT	
POSITIVE	39	1	40
NEGATIVE	1	15	16
TOTAL	40	16	56

SENSITIVITY = 97.5 %

SPECIFICITY = 93.75 %

ACCURACY = 96.43 %

% OF FALSE NEGATIVES = 2.5 %

% OF FALSE POSITIVES = 6.25 %

EFFICACY OF CYTOLOGY IN DIAGNOSIS OF MALIGNANCY

NON ASPIRATION CYTOLOGY :

CYTOLOGY REPORT	HPE REPORT		TOTAL
	MALIGNANT	NON MALIGNANT	
POSITIVE	44	2	46
NEGATIVE	1	22	23
TOTAL	45	24	69

SENSITIVITY = 97.77 %

SPECIFICITY = 91.66 %

ACCURACY = 95.65 %

% OF FALSE NEGATIVES = 2.22 %

% OF FALSE POSITIVES = 8.33 %

SUMMARY

1) Total number of cases studied – 289

2) 58.8 % of the cases were benign lesions, whereas malignancies accounted for 41.2 % of the cases.

3) Most common histological diagnosis was Follicular adenoma (42.6 %).

4) Papillary carcinoma (28.8 % of all cases) was the most common among the malignancies.

5) Male to Female ratio – 1: 7.5, females constituted 88 % of total cases; the male to female ratio for malignancies was 1: 4.

6) Malignancies account for 68 % of histological diagnosis in males and 38 % in females.

7) Overall thyroid swellings were more common in the 21 to 30 years age group.

8) Benign lesions were more common in the age group of 21 to 30 years, whereas Malignancies were more common in the age group of 31 to 40 years.

9) Sensitivity & Specificity of FNAC were 97.5 % and 93.75 % whereas those for FNNAC were 97.77 % and 91.66 % respectively.

10) Overall the Diagnostic Accuracy of FNAC and FNNAC for malignancy of thyroid were observed as 96.43% & 95.65% respectively.

11) For both benign and malignant smears, more number of diagnostically

superior smears were obtained with Non aspiration technique (44.59 % overall) when compared to Aspiration technique (16.26 %).

12) Among the malignant smears 17.5% were Diagnostically Superior in the Aspiration group whereas the same for Non-aspiration group was 41.3%.

13) The Inadequate smears constituted 14.18% & 2.02% of the total number of smears respectively for Aspiration and Non-aspiration techniques.

STATISTICAL ANALYSIS

AGE DISTRIBUTION:

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
AGE * VAR00001	289	100.0%	0	.0%	289	100.0%

Report

AGE

VAR00001	Mean	N	Std. Deviation	Median	Minimum	Maximum	Range
FNAC	35.67	141	12.34	35.00	14	70	56
FNNAC	35.93	148	12.19	35.00	18	70	52
Total	35.81	289	12.24	35.00	14	70	56

p =0.858- not significant

SEX DISTRIBUTION:

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
SEX * VAR00001	289	100.0%	0	.0%	289	100.0%

SEX * VAR00001 Crosstabulation

Count

		VAR00001		
		FNAC	FNNAC	Total
SEX	F	125	130	255
	M	16	18	34
Total		141	148	289

p = 0.488 – not significant

SMEAR CATEGORY:

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
SMEAR CATEGO * VAR00001	289	100.0%	0	.0%	289	100.0%

SMEAR CATEGORY * VAR00001 Crosstabulation

Count

		VAR00001		
		FNAC	FNNAC	Total
SMEAR CATEGORY	THY I	20	3	23
	THY II	16	23	39
	THY III	51	61	112
	THY IV	14	15	29
	THY V	40	46	86
Total		141	148	289

p = 0.005 significant

More FNAC smears turned out to be THY I Category.

Difference was statistically significant.

SMEAR QUALITY:

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
SMEAR QUALIT * VAR00001	289	100.0%	0	.0%	289	100.0%

SMEAR QUALITY * VAR00001 Crosstabulation

Count

		VAR00001		
		FNAC	FNNAC	Total
SMEAR QUALITY	DA	98	79	177
	DS	23	66	89
	UNS	20	3	23
Total		141	148	289

p<0.001 significant

More FNAC smears were of UNS Category.

Difference was statistically significant.

REVIEW OF LITERATURE

In our study of 289 cases, the sex incidence and age specific incidences conform to the epidemiological data given in the literature. Among the histological diagnosis, malignancy accounted for about 41 % of the cases. This proportionately large number of malignant histologies observed may be attributed to the fact that the study was conducted not in community but in a tertiary center, where more malignant and suspicious of malignant lesions were referred from peripheral and secondary level health care.

False-Negative Diagnoses:

False-negative results mean missed malignancy. The false-negative rate is defined as the percentage of patients with "benign" cytology in whom malignant lesions are later confirmed on thyroidectomy. False-negative rates generally vary from 1.5% to 11.5% (average, <5%). The frequency of false-negative cytological diagnosis depends on the number of patients who subsequently have surgery and histological review. In most retrospective series, less than 10% of patients with a benign cytological diagnosis subsequently have thyroid surgery, suggesting that false-negative rates should be interpreted with some scepticism. Despite this note of caution, most authorities agree that the true false-negative rate is less than 5% if all

patients have thyroid surgery. The incidence of false negatives observed with two techniques Aspiration and Nonaspiration (2.5% & 2.22% respectively) in our study was in the range conforming to the standards given in the literature.

False-Positive Diagnoses:

A false-positive diagnosis indicates that a patient with "malignant" FNA results was found on histological examination to have benign lesions. False-positive rates vary from 0 to 8% (average, 3%). The false positivity observed in our study were 6.25% & 8.33% respectively for Aspiration and Non-aspiration techniques that were relatively high when compared to the literature.

Causes of False Diagnoses:

Interpretive or sampling errors account for false diagnoses. Hashimoto's thyroiditis probably is the most common cause of false-positive cytology. Misclassification of follicular and Hürthle cell adenomas as papillary carcinomas accounts for other errors. FN Biopsy of thyroid lymphomas may

produce lymphocytes that can be interpreted as Hashimoto's thyroiditis, accounting for a false-negative diagnosis.

Inadequate or improper sampling accounts for some false-negative errors. For example, nodules smaller than 1 cm in size may be too small for accurate needle placement, and nodules larger than 4 cm in diameter are too large to allow proper sampling from all areas, thereby increasing the likelihood of misdiagnosis.

Review of the literature reveals that the sensitivity of FNA ranges from 65% to 98% (mean, 83%), and specificity ranges from 72% to 100% (mean, 92%). The predictive value of a positive or suspicious cytological result is approximately 50%. The overall accuracy for cytological diagnosis approaches 95%. The sensitivity and specificity of FNAC in our study was 97.5 % & 93.75 % respectively.

In a review by Gharib and Goellner [17,18] of 18,183 FNA biopsies from seven large series, sensitivity rates of thyroid FNA range from 65% to 98% (mean, 83%) and specificity from 72% to 100% (mean 92%).

In a review of 2,595 thyroid aspirates from 11 series in which all patients underwent surgery, Molitch [19] et al reported a false-negative rate of 2%, a 5.4% false-positive rate, and a 22% malignancy rate in the group diagnosed as follicular neoplasm or suggestive of neoplasm.

Study conducted by Seyed Mohammad Tavangar et al [20] in 200 patients concluded that there was no statistically significant difference between FNNA and FNA average scores in each parameter, as noted in our study.

The non-aspiration technique in 36 benign lesions and 13 neoplasms in a study conducted by Santos JE et al [21] obtained diagnostically superior specimens significantly more frequently, similar to the results obtained in our study.

Study conducted by Kamal MM et al [22] concluded that although FNC sampling was diagnostic in a greater number of cases than FNA sampling, there was no proof of clear superiority of FNC over FNA. Until greater experience shows clear sampling superiority of FNC alone, rather than performing only FNA in diffuse or nodular thyroid lesions, incorporating FNC into the second puncture will definitely improve the quality and quantity of material at the patient's first visit. The same conclusion was derived in our study also.

Diagnostically superior specimens were obtained significantly more frequently by the non-aspiration technique as concluded by Rizvi S A et al [23] in a study of 150 patients.

Implementation and adherence to of specific protocols such as an immediate FNA interpretation service, standardizing FNA diagnostic terminology,

based on error reduction initiatives would result in improvement of specimen quality and fewer diagnostic errors, as shown by Stephen S.R. [34].

DISCUSSION

The thyroid gland was selected for the study of Non-aspiration technique, as it is a vascular organ that frequently produces heavily blood stained aspirates. Furthermore, many diagnostic pitfalls exist in the interpretation of thyroid specimens, making excellence of cellular material a prerequisite for diagnosis.

In our study age and sex distribution was statistically analyzed between the two groups and was found to be equally distributed between the two. There was no statistically significant variation in the age and sex distribution between the two populations. (p values for age & sex distribution were 0.858 & 0.488 respectively between the two populations).

In our study, it was observed that the non-aspiration technique yielded more diagnostically superior specimens, as compared with FNA. The number of unsuitable smears was also greater in aspiration samples, as

compared with the non-aspiration technique. The difference was statistically significant ($p = 0.005$).

In our study, no significant difference between the performances of these two techniques was noted, with respect to making a cytological diagnosis of thyroid swellings.

Although the presence of blood cannot be entirely prevented in thyroid cytology samples, its effect on smear quality is minimized by the spontaneous capillary action of the non-aspiration technique as opposed to the active, often high suction pressures of conventional FNA procedures. The cellular material is more concentrated, less traumatized and less obscured by blood or distorted within blood clots in the non-aspiration smears. It also offers many other advantages. Fewer patients complain of pain or discomfort. The technique is simple, easy to perform and enables an enhanced appreciation of the consistency of the mass being sampled. No complications were encountered in any of the patients sampled by the non-aspiration technique. The only disadvantage being acellularity, was noticed in three patients in our study.

Thus the diagnostic accuracy of thyroid cytology in interpretation of malignancy primarily depends on various other factors irrespective of the technique employed being Aspiration or Non-aspiration.

FN CYTOLOGY GUIDELINES

Hossein Gharib et al [18] **has proposed the following guidelines that improve accuracy of Fine-Needle Biopsy (FNB):**

1) Individuals who have had training in both thyroid examination and thyroid biopsy, such as Endocrinologists, should perform FNB. In the hands of experienced operators FNB achieves high diagnostic accuracy.
2) Aspirates should be obtained from different portions of the nodule, preferably peripheral areas, in an organized and sequential manner. It is essential to ensure that an adequate number of follicular cells is present.
3) Particular care to be taken with small (< 1 cm) or large (> 4 cm) nodules because of increased chance of misdiagnosis. USG-guided FNB improves accuracy in this regard.
4) A cytopathologist, preferably one with experience in thyroid cytology, should review and interpret the slides.

5) Non-diagnostic cytology is not negative because as much as 5%-10% of non-diagnostic nodules harbour malignancy.
6) Repeat Biopsy is mandatory if cytology is non-diagnostic, because one-half of previous non diagnostic lesions will be diagnostic on reaspiration
7) If reaspiration yields insufficient material, US-guided FNB is the next test. In the event that the final result is still insufficient, surgical excision is warranted for most nodules.
8) Nodules yielding ”suspicious" cytology should be recommended for excision as there is 10%-30% chance of malignancy
9) Any clinically suspicious, cytologically benign nodule should be recommended for excision and cytology is considered false-negative until proved otherwise in these lesions

In a recent review of thyroid FNA**, Belfiore and La Rosa** suggested the following steps to reduce false-negative results:

- Acquire and maintain adequate biopsy expertise
- Avoid making a diagnosis with a sub optimal sample
- Be cautious with cystic degeneration, Hurthle cells, or lymphocytes
- Repeat FNA at least once during follow-up.

CONCLUSION

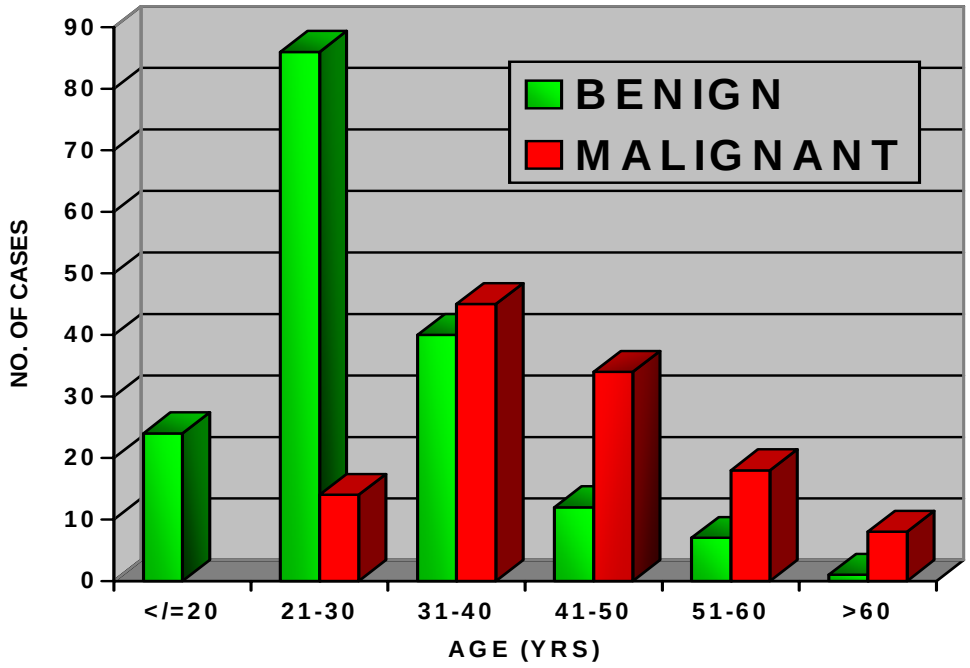
Although no significant difference was seen in the efficacy and diagnostic accuracy of the two techniques in evaluation of thyroid swellings, the non aspiration technique has got it's own merits.

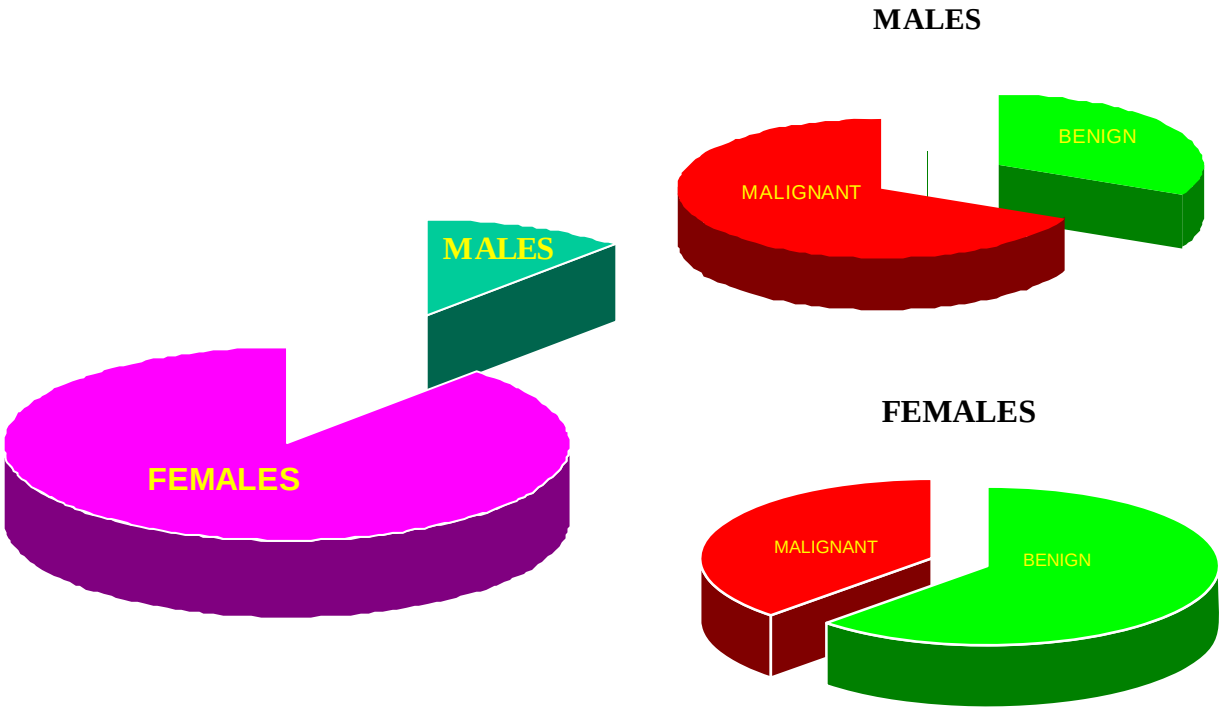
The non-aspiration technique is simple, easy to perform and produces better results in the form of a better quality of the cellularity and less field obscurity by blood in both neoplastic and non-neoplastic lesions of the thyroid. It has statistically significant less chances of producing non-diagnostic smears. The technique is free of complications and very much comfortable to the patient.

Hence, this technique should be used alone or in tandem with FNAC for better diagnostic yield.

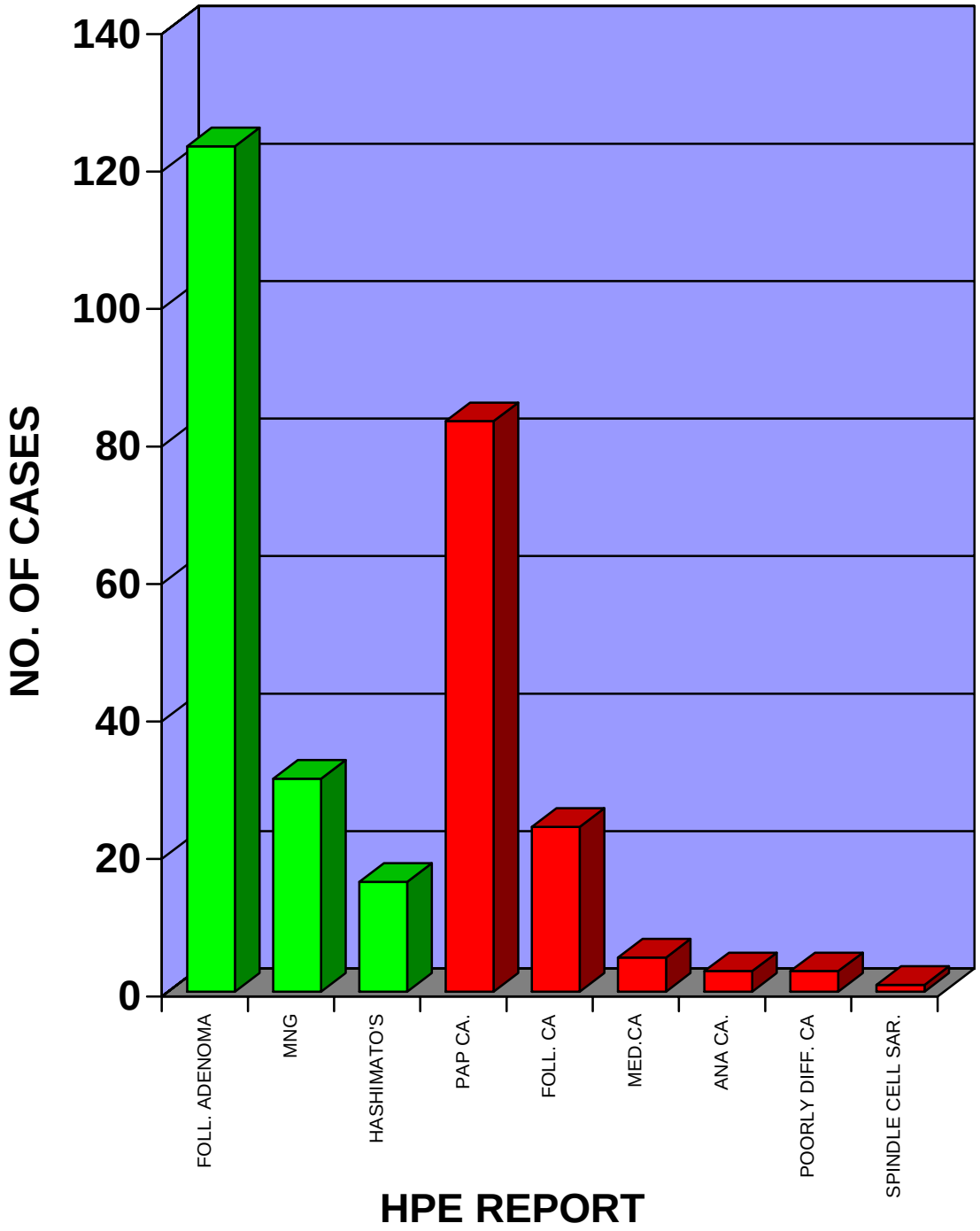
Adhering to a set of guidelines would serve to improve the accuracy of cytodiagnosis irrespective of the technique and enable better evaluation and management of thyroid swellings.

AGE & SEX INCIDENCE





HISTOLOGY DIAGNOSIS



ogical features in common Thyroid Lesions

OGICAL OSIS	COLLOID	CEEL ARRANGEMENT	NUCLEUS	CYTOPLASM	MISCELLAN
LAR RE	Scant to abundant groups, microfollicles	Monolayers	Pyknotic	Ill defined commonly	Cystic change
NIC IDITIS	Absent	Isolated, clusters Hyperplastic changes	Degenerative	Degenerative &/or hyperplastic changes	
OMA	Absent to scanty	Microfollicles Clusters	Enlarged, with overlapping nucleoli	Scanty	Cystic change
ULAR NOMA	Usually absent	Microfollicles Clusters	Enlarged, anisinucleosis, atypical, overlapping nucleoli	Scanty	
LARY NOMA	Scanty or absent	Monolayers, papillae Microfollicles	Enlarged, grooves, ground glass type, inclusions	Ill defined to abundant	Psammomas,
LARY NOMA	Absent	Isolated, small clusters	Eccentric, round or elongated, hyperchromatic	Polygonal, spindle shaped azurophillic granules	Amyloid
ASTIC NOMA	Absent	Isolated, clusters	Giant or spindle shaped, atypical, large nucleoli,	Pleomorphic	Necrosis
E CELL ON	Absent	Isolated, microfollicles	Vesicular, anisonucleosis, prominent nucleoli	Large, pleomorphic, metachromatic granules	

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MASTER CHART FNAC

S.NO.	NAME	AGE	SEX	I.P.NO.	SMEAR CATEGORY	HPE DIAGNOSIS
1	DEVAMANOHARI	42	F	222964	THY V	PAP CA
2	KRISHNAVENI	28	F	399406	THYII	MNG
3	KALYANI	42	F	392153	THY II	FOLL.ADENO.
4	VIJAYA	40	F	396962	THY I	FOLL.ADENO.
5	LAKSHMI	38	F	208813	THY V	PAP CA
6	AMUDHA	23	F	206747	THY II	HASHIMATO'S
7	MUTHAMMAL	26	F	205090	THY III	FOLL.ADENO.
8	PADMA	30	F	375813	THY III	FOLL.ADENO.
9	KOOTHAR	59	M	291704	THY IV	FOLL.CA.
10	MOHANAVALLI	45	F	396388	THY V	PAP CA
11	SUMATHY	22	F	395960	THY I	FOLL.ADENO.
12	SUMATHY	35	F	394695	THY II	MNG
13	PARVATHY	21	F	396074	THY II	MNG
14	KANTHIMATHI	39	F	395522	THY I	FOLL.ADENO.
15	NIRMALA	27	F	393465	THY V	PAP CA
16	SHANTHI	26	F	194269	THYIII	FOLL.ADENO.
17	JEEVA	26	F	385684	THY III	FOLL.ADENO.
18	KARUPANNAN	70	M	294089	THY V	ANAPLASTIC CA
19	PANJAMMAL	33	F	376598	THY V	PAP CA
20	SUMATHY	37	F	377641	THY III	FOLL.ADENO.
21	KALANJIYAM	30	F	374221	THY III	FOLL.ADENO.
22	VEERAMMAL	52	F	165989	THY IV	FOLL.CA.
23	MUTHULAKSHMI	30	F	372434	THY II	HASHIMATO'S
24	SUBBULAKSHMI	40	F	371714	THY III	FOLL.ADENO.
25	YASMIN	14	F	371075	THY I	FOLL.ADENO.
26	VALLI	35	F	151367	THY V	PAP CA
27	CHITRAN	60	M	291453	THY V	PAP CA
28	DHANALAKSHMI	33	F	365956	THY III	FOLL.ADENO.
29	PANCHU	20	F	370529	THY II	HASHIMATO'S
30	PONMANI	36	F	144129	THY V	PAP CA
31	LAKSHMI	19	F	135693	THY I	FOLL.ADENO.
32	MAAREESWARI	30	F	369331	THY II	MNG
33	LINGAMMAL	30	F	141706	THY III	FOLL.ADENO.
34	KODEESWARI	23	F	141227	THY II	PAP CA
35	LOORTHUMARY	42	F	352216	THY III	FOLL.CA.
36	KALIMUTHU	40	M	297005	THY III	FOLL.ADENO.
37	LAKSHMI	30	F	360685	THY V	PAP CA
38	SHANTHI	19	F	360210	THY I	FOLL.ADENO.
39	MEENA	30	F	364810	THY III	FOLL.ADENO.
40	PONMAARIAMMAL	35	F	365929	THY I	PAP CA
41	MEENAKSHI	50	F	355360	THY IV	FOLL.CA.
42	BACKIALAKSHMI	35	F	353640	THY III	FOLL.ADENO.
43	SEKAR	40	M	310291	THY V	PAP CA
44	CHELLAMMAL	55	F	358995	THYIII	FOLL.ADENO.
45	MUMTAJ	35	F	100627	THY I	SPINDLE CELL SAR.
46	PONNEESWARI	29	F	395318	THYIII	FOLL.ADENO.
47	LATHA	33	F	334667	THY V	PAP CA
48	AMMAPONNU	48	F	295526	THY V	PAP CA
49	RAMUTHAI	50	F	295961	THY I	FOLL.ADENO.
50	RAMAMMAL	42	F	395735	THY V	PAP CA

MASTER CHART FNAC

51	PANDIAMMAL	22	F	353608	THY II	HASHIMATO'S
52	SELVI	23	F	352035	THY III	FOLL.ADENO.
53	PITCHAIAMMAL	18	F	352150	THY II	MNG
54	KOLUSAMMAL	35	F	351244	THY III	FOLL.ADENO.
55	MAYAKKAL	60	F	352170	THY IV	FOLL.CA.
56	KADAMBU	55	M	318209	THY V	PAP CA
57	USHA	42	F	944521	THY I	FOLL.ADENO.
58	ESWARI	20	F	271348	THY III	FOLL.ADENO.
59	PANDIAMMAL	50	F	346025	THY V	PAP CA
60	ALFONSA	47	F	346254	THY III	FOLL.CA.
61	KAVITHA	26	F	340021	THY I	FOLL.ADENO.
62	PERUMAL	56	M	104995	THY IV	FOLL.CA.
63	LAKSHMI	38	F	343006	THY IV	HASHIMATO'S
64	ROJA	20	F	361684	THY III	FOLL.ADENO.
65	PONMALAR	25	F	357363	THY V	PAP CA
66	AMARAVATHY	40	F	357149	THY V	PAP CA
67	AMINAAMMAL	20	F	357062	THY III	FOLL.ADENO.
68	JOTHILAKSHMI	21	F	343013	THY III	FOLL.ADENO.
69	VELLAIYAMMAL	39	F	339743	THY III	FOLL.CA.
70	GNANAMMAL	55	F	337442	THY V	PAP CA
71	MENAKA	25	F	337402	THY I	FOLL.ADENO.
72	KAVITHA	25	F	474401	THY II	MNG
73	KAALIAMMAL	37	F	335809	THY III	FOLL.ADENO.
74	PAVANRAJ	46	M	104086	THY IV	MEDULLARY CA.
75	KANAKARATHINAM	67	F	342118	THY III	FOLL.ADENO.
76	LAKSHMI	45	F	331684	THY V	PAP CA
77	RANJANI	18	F	332690	THY I	FOLL.ADENO.
78	SHANTHI	25	F	821139	THY III	MNG
79	MARAGADAM	40	F	327915	THY V	PAP CA
80	ROZIA BEGUM	55	F	327409	THY III	FOLL.ADENO.
81	NATCHAMMAL	25	F	327854	THY V	PAP CA
82	LAKSHMI	45	F	326417	THY III	FOLL.CA.
83	NATARAJAN	35	M	329065	THY V	HASHIMATO'S
84	RATHINAM	35	F	327211	THY V	PAP CA
85	SHANTHI	38	F	325861	THY III	FOLL.ADENO.
86	PONNAMMAL	19	F	318268	THY I	FOLL.ADENO.
87	PANCHAVARNAM	26	F	318279	THY IV	HASHIMATO'S
88	PALANISAMY	61	M	371748	THY V	PAP CA
89	SUMATHY	27	F	309080	THY III	FOLL.ADENO.
90	CHANDRA	32	F	302716	THY III	FOLL.ADENO.
91	PUSHPAM	55	F	304787	THY III	FOLL.CA.
92	MALLIKA	32	F	302677	THY V	PAP CA
93	RENUGADEVI	25	F	269642	THY I	FOLL.ADENO.
94	DEVI	36	F	270273	THY V	PAP CA
95	RAKKAMMAL	35	F	264774	THY III	FOLL.ADENO.
96	KOTHAIAMMAL	46	F	264743	THY II	MNG
97	KARUPAYEE	30	F	262936	THY III	FOLL.ADENO.
98	MANJAMADEVI	29	F	273799	THY V	PAP CA
99	CHELLAMMAL	45	F	271320	THY I	FOLL.ADENO.
100	JYOTHI	20	F	275980	THY II	HASHIMATO'S

MASTER CHART FNAC

101	PERIYAKARRUPPAN	32	M	408704	THY III	FOLL.ADENO.
102	MURUGESHWARI	23	F	276778	THY V	PAP CA
103	MUNIAMMAL	35	F	270191	THY III	FOLL.ADENO.
104	AYYAMMAL	60	F	274421	THY IV	POORLY DIFF. CA
105	PARAMESHWARI	19	F	277432	THY III	FOLL.ADENO.
106	SANTHANALAKSHMI	50	F	278526	THY III	FOLL.ADENO.
107	VELU	58	M	426518	THY V	PAP CA
108	SUGANYA	31	F	278481	THY II	MNG
109	RANI	30	F	282122	THY V	PAP CA
110	VADIVAMMAL	30	F	276291	THY I	FOLL.ADENO.
111	SUSHEELA	27	F	287882	THY III	FOLL.ADENO.
112	RAKKAMMAL	57	F	292392	THY V	PAP CA
113	FATHIMA BEEVI	37	F	310728	THY III	FOLL.ADENO.
114	KALA	22	F	298217	THY III	HASHIMATO'S
115	ASHA DEVI	29	F	294720	THY V	PAP CA
116	HELEN	21	F	297219	THY III	FOLL.ADENO.
117	SONAI	40	M	526146	THY IV	MNG
118	DEVAVINODINI	42	F	222964	THY I	FOLL.ADENO.
119	MAYAKKAL	28	F	232924	THY V	PAP CA
120	ROJA	20	F	161684	THY III	FOLL.ADENO.
121	DURGADEVI	21	F	404073	THY III	FOLL.ADENO.
122	LAKSHMANAN	38	M	173471	THY V	PAP CA
123	VASANTHA	45	F	390761	THY IV	MNG
124	VELLATHAI	65	F	237986	THY IV	FOLL.CA.
125	PANDIAMMAL	30	F	241695	THY I	FOLL.ADENO.
126	MANJULA	30	F	242104	THY III	FOLL.ADENO.
127	CHINAMMAL	43	F	241741	THY IV	MEDULLARY CA.
128	VAIRAVALLI	38	F	242384	THY III	FOLL.ADENO.
129	VANITHA	18	F	235387	THY III	FOLL.ADENO.
130	GEETHA	36	F	323347	THY V	PAP CA
131	REVATHY	23	F	247183	THY III	FOLL.ADENO.
132	DHANAM	48	F	252309	THY V	PAP CA
133	PUSHPAM	37	F	252269	THY I	FOLL.ADENO.
134	GANESAN	30	M	290407	THY III	FOLL.ADENO.
135	VELLAIYAMMAL	40	F	254166	THY V	PAP CA
136	ARUNA	38	F	252728	THY III	FOLL.ADENO.
137	VENNILA	20	F	252473	THY III	FOLL.ADENO.
138	CHELLAMMAL	55	F	411375	THY IV	MNG
139	RAGAVAN	40	M	403443	THY V	PAP CA
140	KAATHAMMAL	54	F	416506	THY V	PAP CA
141	SATHYA	25	F	270861	THY II	FOLL.ADENO.

MASTER CHART FNAC

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MASTER CHART FNNAC

S.NO.	NAME	AGE	SEX	I.P.NO.	SMEAR CATEGORY	HPE DIANOSIS	SMEAR QUALITY
1	RAJATHI	25	F	411733	THY II	MNG	DS
2	LEELAVATHY	28	F	412925	THY III	FOLL.ADENO.	DS
3	JAILANI	40	F	213369	THY V	PAP. CA.	DS
4	ADAIKIYAMMAL	28	F	291200	THY III	FOLL.ADENO.	DA
5	AMUTHA	19	F	410929	THY II	MNG	DS
6	VASANTHA	28	F	233702	THY III	FOLL.ADENO.	DS
7	POONGKODI	37	F	417450	THY I	PAP. CA.	UNS
8	MAHALINGAM	68	M	418720	THY V	ANAPLASTIC CA.	DS
9	ESWARI	24	F	317405	THY III	FOLL.ADENO.	DS
10	ANNAPOORNI	30	F	418713	THY III	FOLL.ADENO.	DS
11	SUBBULAKSHMI	40	F	324404	THY V	PAP. CA.	DA
12	KAALEESWARI	37	F	417449	THY V	PAP. CA.	DA
13	SUMATHY	18	F	425675	THY III	FOLL.ADENO.	DS
14	PUSHPALATHA	30	F	421383	THY IV	MNG	DA
15	NISHA	23	F	310106	THY III	FOLL.ADENO.	DS
16	SORNALATHA	19	F	311106	THY III	FOLL.ADENO.	DA
17	PONNUTHAI	40	F	331016	THY V	PAP. CA.	DS
18	POOMATHY	50	F	429559	THY II	FOLL.ADENO.	DS
19	MURUGESWARAN	30	M	426982	THY III	FOLL.ADENO.	DS
20	PREMA	41	F	436572	THY V	PAP. CA.	DA
21	KAALIATHAL	50	F	436812	THY V	PAP. CA.	DA
22	MUTHUMARI	28	F	436603	THY II	MNG	DS
23	AMIRTHAM	45	F	428449	THY III	FOLL.CA	DA
24	CHINNAMMAL	30	F	239106	THY III	FOLL.ADENO.	DS
25	JEEVARANI	33	F	432106	THY III	FOLL.ADENO.	DA
26	RAVICHANDRAN	41	M	381412	THY V	PAP. CA.	DA
27	POTHIAMMAL	55	F	325106	THY III	FOLL.ADENO.	DS
28	DHANALAKSHMI	41	F	223106	THY V	PAP. CA.	DS
29	ALAGAMMAL	35	F	326106	THY III	FOLL.CA	DA
30	VIJAYALAKSHMI	30	F	527106	THY IV	MNG	DA
31	MUTHAMMAL	60	F	433856	THY III	FOLL.ADENO.	DS
32	LAKSHMI	40	F	429996	THY IV	MEDULLARY CA	DS
33	DHANALAKSHMI	23	F	433853	THY III	FOLL.ADENO.	DA
34	MURUGAVALLI	35	F	320106	THY V	PAP. CA.	DA
35	SHANTHY	33	F	344618	THY II	MNG	DS
36	BALAIAH	48	M	367106	THY IV	FOLL.CA	DS
37	LAKSHMI	22	F	213106	THY III	FOLL.ADENO.	DA
38	GANDIMATHY	24	F	242829	THY III	FOLL.ADENO.	DS
39	MUTHULAKSHMI	38	F	319106	THY V	PAP. CA.	DA
40	JANAKI	35	F	213806	THY III	FOLL.ADENO.	DS
41	KAMATCHI	45	F	438181	THY III	FOLL.ADENO.	DA
42	RAJENDRAN	50	M	372106	THY V	POORLY DIFF. CA	DS
43	SARANYADEVI	26	F	386550	THY III	FOLL.ADENO.	DA
44	RAJESHWARI	48	F	431306	THY V	PAP. CA.	DA
45	PUSHPAVATHY	27	F	273674	THY II	MNG	DS
46	INDUMATHY	26	F	438677	THY II	HASHIMATO'S	DS
47	ALAGAMMAL	46	F	276361	THY V	PAP. CA.	DS
48	MAHALAKSHMI	31	F	890801	THY I	MNG	UNS
49	JEYALAKSHMI	43	F	439477	THY V	PAP. CA.	DA
50	SENNAKRISHNAMMAL	40	F	352106	THY V	PAP. CA.	DA

MASTER CHART FNNAC

51	MEENAKSHI	35	F	378202	THY III	FOLL.CA	DA
52	SUBBULAKSHMI	34	F	321556	THY III	FOLL.ADENO.	DS
53	DASS	59	M	329206	THY V	PAP. CA.	DA
54	SELVI	50	F	350426	THY V	PAP. CA.	DA
55	KRISHNALEELA	29	F	285392	THY II	MNG	DS
56	VIJAYALAKSHMI	40	F	360206	THY III	FOLL.ADENO.	DA
57	ANANDAVALLI	40	F	388464	THY V	PAP. CA.	DS
58	SHANTHY	30	F	442804	THY II	FOLL.ADENO.	DS
59	MUTHALAGU	37	F	370206	THY V	PAP. CA.	DA
60	SATHYA	18	F	169206	THY II	HASHIMATO'S	DS
61	PANDIAMMAL	35	F	437519	THY V	PAP. CA.	DA
62	DEVI	70	F	445039	THY IV	FOLL.CA	DA
63	VIGNESH	18	M	450853	THY II	HASHIMATO'S	DS
64	KAMATCHI	45	F	438687	THY III	FOLL.ADENO.	DS
65	RAJESHWARI	40	F	177500	THY V	PAP. CA.	DA
66	VEERALAKSHMI	40	F	375206	THY V	PAP. CA.	DA
67	VELLAIYAMMAL	48	F	391123	THY III	FOLL.CA	DA
68	VEERARAJAMMAL	33	F	390412	THYIII	FOLL.ADENO.	DS
69	SONAI	65	M	276514	THY V	PAP. CA.	DA
70	RADHA	22	F	276106	THY III	FOLL.ADENO.	DS
71	AMEENA	41	F	445145	THY V	PAP. CA.	DA
72	MUTHURAKKU	22	F	277106	THY II	MNG	DS
73	NAGARATHINAM	39	F	191062	THY V	PAP. CA.	DS
74	VIJAYALAKSHMI	45	F	380186	THY III	FOLL.ADENO.	DA
75	DURAIPANDI	70	M	360158	THY V	PAP. CA.	DA
76	BANUPRIYA	36	F	448410	THY III	FOLL.ADENO.	DS
77	FATHIMABEEVI	45	F	190206	THY V	PAP. CA.	DA
78	ROOPINI	18	F	188206	THY II	HASHIMATO'S	DS
79	SUSHEELA	30	F	389106	THY III	FOLL.ADENO.	DA
80	KRISHNAMMAL	70	F	179206	THY V	ANAPLASTIC CA.	DS
81	GANAPATHY	43	M	282378	THY V	MEDULLARY CA	DS
82	SIKKARI	35	F	267313	THY III	FOLL.ADENO.	DA
83	SUNDARI	46	F	268918	THY III	FOLL.CA	DA
84	MURUGESWARI	40	F	376104	THY III	FOLL.ADENO.	DS
85	RITA	45	F	271685	THY III	FOLL.ADENO.	DS
86	NEELAVATHY	40	F	270046	THY V	PAP. CA.	DA
87	GANDIMATHY	38	F	270005	THY V	PAP. CA.	DS
88	INDRA	35	F	273651	THY V	PAP. CA.	DA
89	LAKSHMI	29	F	273816	THY III	FOLL.ADENO.	DS
90	JEEVAKALA	18	F	275321	THY III	FOLL.ADENO.	DA
91	PANDI	30	M	297328	THY IV	MNG	DA
92	PAPPA	32	F	276548	THY III	FOLL.ADENO.	DA
93	MUNEESWARI	28	F	278828	THY II	MNG	DS
94	ARUNA	18	F	276784	THY II	HASHIMATO'S	DS
95	DEVI	24	F	310204	THY II	MNG	DS
96	SULOCHANA	25	F	369104	THY III	FOLL.ADENO.	DA
97	DEEPA	28	F	292209	THY II	PAP. CA.	DA
98	VIJAYA	31	F	300714	THY III	FOLL.ADENO.	DA
99	RAJAMMAL	59	F	298561	THY IV	FOLL.CA	DA
100	GLADIUS	23	M	502104	THY III	FOLL.ADENO.	DA

MASTER CHART FNNAC

101	MALLIKA	52	F	300763	THY V	PAP. CA.	DS
102	CHITRADEVI	29	F	304026	THY III	FOLL.ADENO.	DA
103	DURGA	33	F	292149	THY V	PAP. CA.	DA
104	MAARIAMMAL	65	F	292159	THY IV	POORLY DIFF. CA	DS
105	ANTHONYAMMAL	54	F	294041	THY IV	FOLL.CA	DA
106	UMA MAHESHWARI	29	F	301935	THY II	FOLL.ADENO.	DS
107	MARIAMMAL	20	F	309565	THY III	FOLL.ADENO.	DA
108	MUTHUSAMY	40	M	350104	THY V	MNG	DA
109	DEEPA	23	F	283827	THY III	FOLL.ADENO.	DS
110	MALAR	21	F	219558	THY IV	HASHIMATO'S	DA
111	JEYASUDHA	25	F	283814	THY III	FOLL.ADENO.	DS
112	AYYAMMAL	45	F	283793	THY V	PAP. CA.	DA
113	MUTHURAKKU	18	F	278849	THY I	FOLL.ADENO.	UNS
114	DURGADEVI	40	F	310104	THY III	FOLL.ADENO.	DA
115	RAMALINGAM	45	M	501064	THY V	PAP. CA.	DA
116	CHANDRA	33	F	319910	THY III	FOLL.ADENO.	DA
117	TIRUPATHI	22	F	270860	THY II	MNG	DS
118	PUSHPALATHA	28	F	311248	THY II	MNG	DS
119	LOORTHUMARY	55	F	226484	THY III	FOLL.ADENO.	DA
120	DHANAM	35	F	211360	THY V	PAP. CA.	DS
121	MURUGESWARI	22	F	417140	THY III	FOLL.ADENO.	DA
122	ABDUL KADAR	60	M	268132	THY IV	FOLL.CA	DA
123	ESWARI	25	F	417034	THY III	FOLL.ADENO.	DS
124	VASUKI	32	F	316948	THY V	PAP. CA.	DA
125	PITCHAIAMMAL	58	F	317242	THY IV	FOLL.CA	DS
126	MURUGAN	30	M	387921	THY III	FOLL.ADENO.	DA
127	RAJESHWARI	41	F	227630	THY V	PAP. CA.	DA
128	SHANTHY	38	F	171710	THY V	PAP. CA.	DA
129	SHAKILA BEGUM	32	F	484690	THY III	FOLL.ADENO.	DS
130	MUNEESHWARI	23	F	584671	THY III	FOLL.ADENO.	DA
131	SHANTHY	22	F	134463	THY II	MNG	DS
132	RANI	26	F	729001	THY II	MNG	DS
133	MALLIKA	25	F	526361	THY III	FOLL.ADENO.	DA
134	MAHESHWARI	37	F	261800	THY IV	MEDULLARY CA	DS
135	RAJESHWARI	40	F	582471	THY V	PAP. CA.	DA
136	BACKIALAKSHMI	41	F	580991	THY V	HASHIMATO'S	DA
137	SAVUDAMOORTHY	40	M	350193	THY III	FOLL.CA	DA
138	VALLI	58	F	520823	THY IV	FOLL.CA	DS
139	LEELAVATHY	29	F	175639	THY III	FOLL.ADENO.	DA
140	MURUGESWARI	32	F	486001	THY IV	PAP. CA.	DA
141	NAGAMANI	26	F	485190	THY III	FOLL.ADENO.	DA
142	ALAGU	40	F	260444	THY V	PAP. CA.	DA
143	MATCHADEVI	30	F	435910	THY III	FOLL.ADENO.	DA
144	SUBRAMANI	35	M	260158	THY V	PAP. CA.	DA
145	THERESA	39	F	323241	THY III	FOLL.ADENO.	DA
146	JEYACHITRA	19	F	325581	THY II	MNG	DS
147	VALARMATHI	24	F	332291	THY III	FOLL.ADENO.	DS
148	PRABHA	28	F	330412	THY III	FOLL.ADENO.	DA